

been carefully studied. Reconsideration and allowance are hereby respectfully urged.

Briefly, the present invention relates to isolated DNA molecules which encode naturally occurring human TBP-II. TBP-II is a novel tumor necrosis factor binding protein which is an extracellular domain of a TNF receptor. It was first disclosed in the priority applications of the grandparent application, and one claim directed to this protein was officially found to be allowable by the examiner in charge of the parent case. The claims drawn to the protein in parent application of 07/930,443 are now involved in an interference proceeding with the claims of USP 5,344,915. The present application claims any isolated DNA molecule encoding the novel human TBP-II protein, as well as replicable expression vehicles capable of expressing that protein, host cells transformed with such replicable expression vehicles and processes for producing the protein by culturing such host cells.

The examiner has withdrawn claim 50 from consideration as being directed to an invention that is independent or distinct from the invention originally claimed.

Claim 50 is in the same category as previously appearing claims 14, 39, 42 and 45, which also have previously been withdrawn from consideration. However, with respect to claims 14, 39, 42 and 45, the examiner has indicated that, in the event that the claims currently under consideration are found allowable, the withdrawn claims would be treated as per

MPEP §821.04. It is respectfully requested that the examiner confirm that claim 50 will be treated in the same manner as claims 14, 39, 42 and 45, in the event that the claims currently under consideration are found allowable.

Claims 11-13, 34, 40, 41 and 46-49 have been rejected under 35 USC 112, first paragraph, as containing subject matter which is not described in the specification. The examiner states that there is no support in the specification as originally filed for the recitation of "including the amino acid sequence: Thr-Pro-Tyr-Ala-Pro-Glu-Pro-Gly-Ser-Thr" in claims 11 or 46. The examiner states that the specification discloses that the sequence was determined by "N-terminal sequence analysis" and that this indicates that said sequence is in the N-terminal region of the TBP-II molecule recited in the claim. The examiner states that there is no support for a DNA encoding a molecule in which the sequence is not at the N-terminal and there is no written description of such a molecule in the specification. The examiner states that a preferred substitution would use the language in original claim 6 with regard to the location of the sequence recited in the claim.

Claims 11 and 46 have now been amended to specify that the specified amino acid sequence is "at the N-terminal region thereof". The examiner has conceded that the language in the specification indicates that the sequence is "in the N-terminal region of the TBP-II molecule recited in the claim". This language, while not appearing *in ipsius verbis* in the

specification; is a concept which is fully described in the specification and thus is permissible under the standards of 35 USC 112. Note In re Anderson, 176 USPQ 331, 336 (CCPA 1973), where the Court reversed what was effectively a written description rejection based on appellant's change of the claim terminology "containing a medicant" to "carrying a medicant."

The court reasoned:

The question, as we view it, is not whether "carrying" was a word used in the specification as filed but whether there is support in the specification for employment of the term in a claim; is the concept of carrying present in the original disclosure? We think it is. [Emphasis original]

The examiner concedes that the concept is supported in stating that the language used in the specification indicates that said sequence is in the N-terminal region of the TBP-II molecule. Applicant does not wish to be limited to the language of previously appearing claim 6 as the claim recites the shortest of the various N-terminal truncations disclosed in the specification and it is clearly intended that the claim encompass all of those disclosed N-termini. It should be clearly understood, and it is hereby explicitly stated, that this amendment is being made merely to expedite allowance of the present claims. Applicant does not believe that such amendment is necessary or that it changes the scope of the present claims in any way.

Accordingly, it is believed that the present amendment obviates the concern noted by the examiner in this rejection. Reconsideration and withdrawal thereof are respectfully urged.

Claims 11-13, 34, 40, 41, and 46-49 have been rejected under 35 USC 112, first paragraph, as containing subject matter which is not described in the specification. The examiner states that there is no support in the specification as originally filed for the language "after being purified by affinity chromatography ... when measured by reducing SDS-PAGE". The examiner states that the scope of the claim is not commensurate with the scope of the disclosure. However, the examiner states that original claim 7 recites language describing the purification procedure that has support in the specification as originally filed.

In view of the examiner's indication that the language of claim 7 would be acceptable, claims 11 and 46 have now been amended to use language which is derived from the language of claim 7. It is believed that the wording in present claims 11 and 46 is supported by the written description provided by claim 7 even though the exact sequence of the words is not identical. Note MPEP §2163.02 where it states:

The subject matter of the claim need not be described literally (i.e., using the same terms or *in haec verba*) in order for the disclosure to satisfy the description requirement.

Accordingly, as the language suggested by the examiner has been substantially adopted, reconsideration and withdrawal of this rejection are respectfully urged.

Claims 35, 43 and 44 have been rejected under 35 USC 112, first paragraph, as containing subject matter which is not described in the specification. The examiner states that there

is no support in the specification as originally filed for the claimed molecules as the specification discloses that the features of the TBP-II molecule recited in claim 35 are found in a molecule of 30 kD, but there is no disclosure in the specification of the existence of a TBP-II molecule recited in claim 35 other than one wherein the molecular weight is 30 kD. Thus, the examiner states that the scope of the claimed molecule exceeds the scope of the disclosure of the specification as originally filed. This rejection is respectfully traversed.

Claim 35 does not claim a protein but claims a DNA. The molecular weight of a protein is not particularly relevant when defining a DNA as the same DNA can encode proteins of various molecular weights depending on post-translational glycosylation patterns. Thus, the same DNA can produce a lower molecular weight protein in bacterial hosts and a protein with the exact same sequence with a higher molecular weight in eukaryotic hosts. Furthermore, proteins of identical amino acid sequence can naturally exist in different glycosylation forms resulting in different molecular weights. Claim 35 defines the DNA as encoding a protein having a specified N-terminal amino acid sequence and a specified biological activity. This language adequately defines the protein without having any ambiguity as to molecular weight which can vary depending on glycosylation.

The examiner has not suggested that any naturally occurring protein exists which has a sequence which differs from that of the protein described in the present specification. The

examiner is invited to conduct a homology search on the various presently existing computer databases of naturally occurring human proteins. This will establish that the issue raised by the examiner is an artificial issue and should be dropped. Reconsideration and withdrawal of this rejection are therefore respectfully urged.

Claims 35, 43 and 44 have been rejected under 35 USC 112, first paragraph, as containing subject matter which is not described in such a way as to comply with the enablement requirement. The examiner states that there is no disclosure in the specification of the existence of a TBP-II molecule recited in claim 35 other than one wherein the molecular weight is 30 kD, and there is no evidence that the properties exist except in a 30 kD molecule, and therefore the specification is not enabling for the claimed DNA. This rejection is respectfully traversed.

It is urged that this is an artificial issue for the same reasons as discussed above with respect to the written description requirement based on the same language. The claims are directed to DNA and the DNA is described in an enabling manner regardless of whether or not there is a recitation as to molecular weight for the protein which it encodes. The molecular weight recitation is mere surplussage and need not appear in the claim. The presence or absence of this recitation does not change the scope of the claim and thus does not raise enablement issues. It is inappropriate to include the molecular

weight in such a claim as the molecular weight of a protein depends on factors such as glycosylation. However glycosylated, the nucleotide sequence which encodes it will be the same. Accordingly, reconsideration and withdrawal of this rejection for the same reasons as discussed above with respect to the written description requirement are respectfully urged.

Claims 11-13, 34-38, 40, 41, 43, 44 and 46-49 have been rejected under 35 USC 112, first paragraph, as containing subject matter which is not described in the specification. The examiner states that the specification does not convey to the artisan that the applicant had possession at the time of the invention of the claimed DNAs and molecules containing said DNAs. The examiner states that there is no disclosure in the specification of an intact DNA sequence which encodes said molecule. The examiner states that the claimed invention encompasses genomic DNA but there is no written description of said genomic DNA. The examiner states that the claimed DNA encompasses DNA encoding the TBP-II molecule wherein said molecule is derived from species other than humans while there is no description of such DNA sequences in the specification as originally filed. The examiner states that if an inventor is unable to envision the detailed constitution of a gene so as to distinguish it from other materials, conception has not been achieved until reduction to practice has occurred and that naming a type of material generally known to exist in the

absence of knowledge as to what that material consists of is not a description of that material. This rejection is respectfully traversed.

In an attempt to obviate this rejection, the present claims have now been amended to specify that the DNA encodes the human TBP-II molecule. Thus, the claims no longer read on corresponding molecules of other species and the cited University of California v. Eli Lilly case is no longer applicable. With respect to the examiner's statement that the claimed invention encompasses genomic DNA which might have introns, the examiner raises a valid point and applicant has endeavored to amend the claims so as to exclude sequences with introns. Applicants' written description is based on the sufficient description of a human TBP-II molecule to allow one of ordinary skill in the art to obtain the entire amino acid sequence thereof without undue experimentation. Once the complete amino acid sequence is known, all contiguous DNA sequences which encode such a protein are known in view of the known rules of the genetic code. In order to avoid reading on DNA with introns, the present claims have been amended to specify that the nucleotide sequence coding for TBP-II is "a contiguous nucleotide sequence". While the word "contiguous" does not appear in the present specification, the concept of the DNA being contiguous certainly is present in the present specification and there can be no doubt that applicant has invented all DNA without introns which encodes the protein of



the present invention. Note that the present specification explicitly states, for example at page 8, lines 22 and 23, that the DNA molecules may be "genomic DNA, cDNA, synthetic DNA and combinations thereof." Thus, applicants have conceived synthetic DNA encoding an amino acid sequence, which must inherently be contiguous. The same language appears in the priority application at page 15, lines 16-17. Accordingly, the examiner's concerns about the claims reading on non-disclosed genomic DNA have been alleviated by the present amendment.

The cases cited by the examiner relate to genes, i.e., naturally occurring DNA sequences. The present invention is not directed to the naturally occurring sequence. The present invention is broadly directed to any sequence which encodes the naturally occurring amino acid sequence of the protein of the present invention. Once the protein of the present invention is known, then one is able to envision the detailed constitution of the DNA which encodes such a protein so as to distinguish it from other materials. As argued at length previously in the present prosecution, the protein of the present specification has been sufficiently described to fully define it. This is evidenced by the fact that at least one protein claim has been allowed in the parent application. Accordingly, as the present application places the protein into the hands of the public and one of ordinary skill in the art reading the present specification can determine the complete amino acid sequence without undue experimentation, there is a complete description

of the DNA sufficient to comply with all of the requirements of the Amgen and University of California cases cited by the examiner.

The invention is described, not an indication of a result that one might achieve if one made that invention. The present specification includes much more than a mere outline of goals applicant hopes that the claimed invention achieves and problems the invention will hopefully ameliorate. The present description places into the hands of the public a novel isolated protein and therefore, merely by knowledge of the genetic code, also places into the hands of the public all nucleotide sequences which encode that protein. The examiner's statement about cDNAs is irrelevant as applicant is not claiming a specific naturally occurring cDNA but is claiming all DNAs which encode a particular amino acid sequence, which DNAs can readily be prepared by those of ordinary skill in the art by synthetic means. Accordingly, reconsideration and withdrawal of this rejection are also respectfully urged.

Claims 11-13 and 46-49 have been rejected under 35 USC 112, second paragraph, as being indefinite in the recitation of "apparent molecular weight". The examiner prefers the language of original claim 7.

In order to obviate this rejection, the word "apparent" has now been deleted from the claims. All that had been meant was that such was the molecular weight which is observed. Removal of the word "apparent" does not change the

scope of the claim in any way. As this rejection has now been obviated, reconsideration and withdrawal thereof are respectfully urged.

Claims 11-13, 34-38, 40, 41, 43, 44 and 46-49 have been rejected under 35 USC 102(e) as being anticipated by Smith. The examiner states that this rejection can be overcome by the submission of English-language copies of the foreign priority documents, assuming that the claimed inventions are disclosed in said foreign priority documents. The examiner states, however, that the claims are not supported by the foreign priority documents at least for the same reasons previously presented by the examiner why he does not consider them to be fully supported by the present application. This rejection is respectfully traversed.

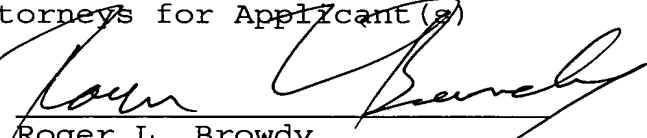
The examiner's attention is respectfully invited to the fact that the priority applications of record in this case are all in the English language. It is not necessary to submit a translation of priority documents which are in the English language. The examiner already has in his hands all of the documentation necessary in order to confirm that the presently amended claims are not only supported by the present application (for the reasons discussed above), but are also supported by the priority application 90,339 filed in Israel on May 18, 1989. If the claims are supported in the May 18, 1989, application, it is not necessary for the examiner to review the other two later filed priority applications.

It is submitted that all of the claims now present in the case clearly define over the references of record. Reconsideration and allowance are therefore earnestly solicited.

Respectfully submitted,

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